EMA/631923/2020

European Medicines Agency decision

P/0500/2020

of 22 December 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for (R)-2-(1-(6-Amino-5-chloropyrimidine-4-carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin-2-yl)thiazole-5-carboxamide (DAY101) (EMEA-002763-PIP01-20) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by DOT Therapeutics-1 Inc on 21 February 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 November 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006, and of its own motion in accordance with Article 21 of said Regulation for the deferral, and in accordance with Article 13 of said Regulation for the waiver,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for (R)-2-(1-(6-Amino-5-chloropyrimidine-4-carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin-2-yl)thiazole-5-carboxamide (DAY101), tablet, age-appropriate oral formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for (R)-2-(1-(6-Amino-5-chloropyrimidine-4-carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin-2-yl)thiazole-5-carboxamide (DAY101), tablet, age-appropriate oral formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for (R)-2-(1-(6-Amino-5-chloropyrimidine-4-carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin-2-yl)thiazole-5-carboxamide (DAY101), tablet, age-appropriate oral formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to DOT Therapeutics-1 Inc, 395 Oyster Point Boulevard, Suite 217, 94080 - South San Francisco, USA.

EMA/PDCO/452262/2020
Amsterdam, 13 November 2020

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002763-PIP01-20

Scope of the application

Active substance(s):

(R)-2-(1-(6-Amino-5-chloropyrimidine-4-carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin-2-yl)thiazole-5-carboxamide (DAY101)

Condition(s):

Treatment of paediatric low grade glioma

Pharmaceutical form(s):

Tablet

Age-appropriate oral formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

DOT Therapeutics-1 Inc

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, DOT Therapeutics-1 Inc submitted for agreement to the European Medicines Agency on 21 February 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 31 March 2020.

Supplementary information was provided by the applicant on 7 August 2020. The applicant proposed modifications to the paediatric investigation plan and waiver.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral of its own motion in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of paediatric low grade glioma

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- tablet, age-appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of paediatric low grade glioma

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsed or refractory patients with low grade glioma harbouring BRAF fusion

Treatment of patients newly diagnosed with unresectable or sub-totally resected low-grade glioma harbouring BRAF fusion

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablet, age-appropriate oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1 Development of an age-appropriate oral formulation.
Non-clinical studies	0	Not applicable.
Clinical studies	3	Study 2 A dose finding study of DAY101 in children with low grade gliomas and other RAS/RAF/MEK/ERK pathway activated tumours, as the basis for determination of the posology to be confirmed in study 3.

Area	Number of measures	Description
		Study 3 Open-label, single arm trial, to evaluate pharmacokinetics, safety and activity of DAY101 in children from 6 months to less than 18 years of age (and adults up 25 years) with relapsed or progressive low grade glioma harbouring BRAF fusions. Study 4 Randomised controlled trial to evaluate safety and efficacy of DAY101 in children from 6 months to less than 18 years of age (and adults up to 25 years) with newly diagnosed unresectable or sub-totally resected low-grade glioma harbouring BRAF fusions.
Extrapolation, modelling and simulation studies	1	Study 5 Modelling and simulation study to confirm or modify the paediatric posology in children from 6 months to less than 18 years of age with low grade glioma.
Other studies	1	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes